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Central Venous Catheter Failures: Nowhere Near Zero

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Central venous access devices (CVADs) offer a critical conduit for the delivery of life-sustaining therapies to patients in the intensive care unit (ICU). The insertion and maintenance of CVADs are associated with considerable morbidity, including, but not limited to, central line associated bloodstream infection (CLABSI), local infection, thrombosis, and dislodgement. Evidence, or even suspicion of these complications, often results in early removal and replacement of the CVAD, exposing the patient to additional procedural risks. Much attention has been given in recent years to quantifying and preventing CLABSIs (1, 2). However, in the literature there is a conspicuous paucity of estimates for CVAD failures (apart from CLABSIs) across all types of catheters. These data are essential to gauge patients' overall burden of risk from such devices.

In this issue of *Critical Care Medicine*, Takashima et al (3) evaluated CVAD failures and complications across the gamut of CVADs in the ICU population by way of meta-analysis spanning 63 studies containing 50,000 CVADs and 396,951 catheter days. The review included randomized controlled trials and observational cohort studies dating back to 2006 and enrolling adults with CVADs in the ICU setting that reported the outcomes of interest. The primary outcome for this meta-analysis was CVAD failure, defined as removal of the device prior to the completion of therapy. The secondary outcomes were CVAD complications after successful insertion defined as CLABSI, catheter related bloodstream infection, catheter-associated venous thrombosis, removal due to suspected infection, occlusion, dislodgement, breakage, local infection, or phlebitis. The authors followed standard operating procedure for systematic reviews which included careful study selection, *a priori* reporting of study design and rigorous assessments of study quality, risk of bias and heterogeneity where possible.

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The study identified that one in every twenty CVADs fail (5%) before the completion of treatment in the ICU. This is an important finding not only in the context of patient safety, but also from the perspective of provider time, hospital resources and healthcare dollars associated with CVAD replacement which could have been put to other use had removal and replacement been obviated. However, one of the more interesting findings in this study was the large number of catheters removed for suspicion of infection in which infection was not able to be confirmed. Of the 1527 catheters removed for suspicion of infection, only 169 catheters could be confirmed as the source, implying that a sizable proportion of these probably did not need to be removed at all. Given that suspicion for infection was the most common reason for CVAD failure, removing such a large proportion of CVADs unnecessarily has broad implications and highlights the need for better diagnostic criteria before removing a critically important indwelling device. This study is also a reminder that meaningful interpretation of incidence and risk of complications requires appropriate matching of the metric to the quantity being measured. For instance, although peripherally-inserted central venous catheter (PICC) lines were found to display the highest proportion of pooled failures, these catheters are generally retained for much longer than other non-tunneled CVADs, allowing for greater exposure time and in fact, using an alternative (and in this case more appropriate) metric, i.e. incidence rate per 1000 catheter days, demonstrated the lowest incidence of pooled failures among PICC lines.

The authors acknowledge some of the limitations of this study, including heterogeneity across studies and within subgroups. Heterogeneity in meta-analyses can be clinical, methodologic or statistical (i.e. whether outcome differences can be explained by chance alone); the latter can be measured using the I^2 statistic whereas the extent of clinical and methodologic heterogeneity is not readily quantifiable (4). The authors report very high statistical heterogeneity for most of their pooled incidence estimates, making interpretation of these pooled rates challenging. Furthermore, subgroup analyses demonstrated a high degree of variance in incidence rate of CVAD complications by ICU and catheter type: for example, within a sizable cohort of patients from ICU's with unreported ICU type, the incidence rate of CVAD complications ranged from 1.1 [95% CI 0.04–2.2] per 1000 catheter days for PICC lines to 19.9 [95% CI 15.5–24.3] per 1000 catheter days for hemodialysis catheters. Such variance is not necessarily bad, but makes comparisons in estimates across centers, health-systems or regions difficult in the absence of complete data and highlights the importance of recording detailed clinical and catheter-specific features in future studies on CVAD complications.

Another intriguing and highly relevant finding of this meta-analysis is that the pooled estimate for CLABSI was 4.59 per 1000 catheter days, which is much higher than the most recent reports by ICU surveillance databases. The National Healthcare Safety Network reported a rate of 1.1 per 1000 catheter days in their most recent report (5). The Michigan Keystone project, which includes 121 ICUs, reported a mean annual CLABSI rate of 2.5 per 1000 catheter days in 2004 which continuously declined over a 10-year period to 0.76 per 1000 catheter days in 2013 (6). The authors noted that their review included multiple studies from countries of lower socioeconomic levels such as Brazil and India, which is associated with higher rates of CLABSI (7). This, they said, may have contributed to their much higher than expected CLABSI rate. However, the authors also note that the CLABSI rate in Europe,

an area of the world that has similar socioeconomic levels to that of the United States (U.S.), was 3.6 per 1000 catheter days (8). This is more than 3 times higher than the rates reported in the U.S. This raises the question as to what the U.S. is doing differently than the rest of the world that contributes to such low CLABSI rates across the U.S.?

The last two decades have witnessed the introduction of several novel technologies such as antibiotic/antiseptic impregnated catheters, chlorhexidine skin antisepsis, and chlorhexidine-impregnated dressings that, when utilized, reduce CLABSI rates (2). Additionally, bundled strategies and an emphasis on education and training for those who insert and maintain catheters have undoubtedly contributed to the reduction in CLABSI rates (9). These strategies have been implemented both in Europe and the U.S. However, unique to the U.S., the Centers for Medicare and Medicaid Services instituted reimbursement at a lower level to hospitals for encounters complicated by CLABSIs and other hospital-associated conditions in 2008. These economic penalties have provided motivation to hospital administrators to aggressively reduce CLABSI rates, which have led some to speculate that creative strategies, new accounting methods, and conscious and/or unconscious bias may be contributing to artificially lowering rates, while not necessarily impacting patient care.

In addition to the non-reimbursement policies instituted in 2008, several states have passed laws over the past 20 years requiring public reporting of hospital acquired infection rates for all hospitals. In 2004, only 4 states had a public reporting requirement but in 2016, 38 states and the District of Columbia required public reporting. It is difficult to ascertain how these reporting requirements impact care at the bedside, but the policy is designed to pressure hospitals to reduce their rates to zero. Economic incentives used as levers to influence behaviors and practices often result in some unintended consequences. One unintended consequence in this setting is that our accounting methods have changed.

The National Healthcare Safety Network definition of CLABSI requires the presence of a laboratory-confirmed bloodstream infection in a patient with a central venous catheter and no identifiable alternative source of bacteremia. The last criterion can be especially subjective. One area of concern is the search for an alternative source of bacteremia that takes place today, but likely did not occur 2 decades ago because there were no financial consequences then, as there are today. Today, the policies of public reporting and non-payment have incentivized a very granular look for other possible sources of bacteremia. CLABSI rates reported in the past 2 decades may have over-estimated the true rates given that searches for other source of bacteremia were not as robust. On the other hand, reported rates today may be *underestimating* CLABSI rates if the definition is not applied rigorously. And even with rigorous application of the definition, inter-rater reliability can be less than optimal (10).

Another change in classifying CLABSIs came in 2013. In an attempt to prevent misclassification of bacteremia caused by oral or gastrointestinal organisms in patients with neutropenia or graft versus host disease, the CDC added another category for laboratory confirmed bloodstream infections. This new category, mucosal barrier injury (MBI), is intended to improve the comparability of CLABSI rates by reducing the number of BSIs that are not associated with the CVC, but would have technically met the definition of

CLABSI(11). Retrospective studies have shown an overall decrease in CLABSI rates when MBI cases were considered separately(12). Thus, whether lower rates after 2013 reflect actual reductions in CLABSIs or are an artifact related to changes in classification remain unclear.

There are many factors that have contributed to an overall reduction in CLABSI rates over the last 20 years. Some factors have had real impact on patient care while others have impacted the numbers by changing our accounting methods. While Takashima et al. correctly concluded that significant advances are needed to reduce the number of catheters removed unnecessarily for suspected infection, this study also shines a light on what the real-world CLABSI and other CVAD complication rates are, and makes a strong case that we also need more accurate and reliable definitions, less susceptible to subjectivity, to enable valid comparisons.

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